

Executive Function Oculomotor Tasks in Girls With ADHD

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ABSTRACT

Objective: To assess executive function in girls with attention-deficit/hyperactivity disorder (ADHD) using oculomotor tasks as possible trait markers for neurobiological studies. **Method:** Thirty-two girls aged 6 to 13 years with *DSM-IV* ADHD and 20 age-matched, normal control girls were tested on a variety of oculomotor tasks requiring attention, working memory, and response inhibition, which included smooth pursuit, delayed response, and go-no go tasks. **Results:** Girls with ADHD performed the delayed response task correctly on 32% of trials as measured by number of memory-guided saccades, in contrast to 62% of trials for control subjects ($p = .0009$). Patients made twice as many commission errors to no go stimuli ($p = .0001$) and 3 times as many intrusion errors (saccades in the absence of go or no go stimuli; $p = .004$) during the go-no go task compared with controls. Smooth pursuit performance was statistically equivalent across subject groups. Repeated testing in a subgroup of 15 patients revealed substantial practice effects on go-no go performance. **Conclusions:** The data confirm that girls with ADHD exhibit impairments in executive function, as has been reported in boys, implying a similar pathophysiology of ADHD in both sexes. However, practice effects may limit the utility of the oculomotor go-no go task for some neurobiological studies. *J. Am. Acad. Child Adolesc. Psychiatry*, 2000, 39(5):644–650. **Key Words:** attention-deficit/hyperactivity disorder, executive function, oculomotor tasks, go-no go, delayed response tasks.

Although attention-deficit/hyperactivity disorder (ADHD) is the most thoroughly researched psychiatric disorder of children, most studies have focused on boys. The scarcity of attention to girls with ADHD is particularly marked in neuropsychological investigations. One early effort contrasted boys with ADHD to girls, but failed to include normal controls (Brown et al., 1991). Another study that included 15 girls with ADHD was focused on comorbidity with Tourette's disorder, and separate analyses for sex by diagnosis were not reported (Schuerholz et al., 1998). A recent pilot study found that 43 girls with ADHD were

more impaired on estimated IQ than comparison subjects, although they did not differ significantly from controls on executive function tasks, leading to the suggestion that "girls with ADHD may be less vulnerable to executive function deficits than boys" (Seidman et al., 1997, p. 366).

Current theories of the pathophysiology of ADHD emphasize impairment in cognitive "executive function" (Barkley, 1997; Denckla, 1989), which is defined as "the ability to maintain an appropriate problem-solving set for attainment of a future goal" (Welsh and Pennington, 1988, p. 201) and is thought to include processes responsible for allowing an individual to initiate, sustain, and shift attention (Denckla, 1996). The possibility that girls with ADHD might be less vulnerable to executive function deficits has implications for understanding the pathophysiology of the disorder in light of documented differences in male/female prevalence (Simonoff et al., 1997; Szatmari, 1992).

A wide range of tasks can be used to investigate neuropsychological function (Pennington and Ozonoff, 1996). Eye movement tasks are attractive because they are non-invasive, can be performed in brief sessions, and allow for the testing of a wide range of task designs, all using essentially intuitive eye movements or suppression of eye

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movements. In this study, we examined 2 tasks that are presumed to require executive function, i.e., go-no go (Trommer et al., 1988) and delayed response (Kojima and Goldman-Rakic, 1982). To control for nonspecific effects, we also included a "simpler" smooth pursuit task on which boys with ADHD had been previously found to perform normally (Jacobsen et al., 1996).

METHOD

Subjects

ADHD Group. A total of 32 females with ADHD (mean age \pm SD, 8.8 ± 1.9 years) were recruited from local clinics and schools. *DSM-IV* diagnoses were based on interview with a parent and separately with the patient if older than 9 years, using the Diagnostic Interview for Children and Adolescents (DICA) (Herjanic and Reich, 1997), the Conners Teacher Rating Scale-Revised (CTRS) (Conners, 1997), and the Teacher's Report Form (Achenbach et al., 1991). Patients were required to meet full *DSM-IV* criteria for combined type ADHD by parental structured interview and to have a CTRS Hyperactivity factor greater than 2 SD above the mean for their age and gender. Exclusion criteria were a Full Scale WISC-III IQ < 80 (Wechsler, 1991), evidence of medical or neurological disorders on examination or by history, Tourette's disorder, or any other Axis I psychiatric disorder requiring psychiatric treatment.

Control Group. Twenty unrelated age-matched girls (9.6 ± 1.7 years) were recruited from the community. Screening included telephone interview and parent and teacher rating scales. In-person assessment consisted of the 12 handedness items from the Revised Physical and Neurological Examination for Subtle Signs (Denckla, 1985) and structured psychiatric interview (DICA-IV). Children were excluded if they met criteria for any psychiatric disorder except simple phobias.

The local institutional review board approved the study, and written informed consent and assent were obtained from a parent and each subject, respectively.

Eye Tracking Procedure

All subjects were administered a battery of eye movement tasks, including the 3 reported here, in a single session in a darkened testing room. For all tasks, subjects were seated 57 cm away from a computer monitor on which the stimuli were presented; their heads were stabilized using individually prepared bite plates. Angular position of the left eye was measured using the Ober2 infrared orbital scanning system, which uses infrared sources and sensors mounted inside goggles (Permobil Meditech, Inc., Woburn, MA). The sensors require no mechanical calibration, which makes them easier to use with children. Electronic calibration was accomplished at the beginning of each new task by having the subject fixate on a series of sequentially presented white square targets (0.3° on a side) displayed on a black background for 2 sec at 7.5° intervals in the horizontal plane across the video monitor. This system uses extremely brief pulses of infrared light at a rate of 600 Hz and collects each data point over a few microseconds; thus its time constant is well under 1 msec.

Eye position data were collected on a Pentium-based computer and transferred to a Unix-based workstation for analysis, where it was first smoothed using a 10-msec box window. Saccades were then identified using an automated procedure that labeled eye position intervals with

peak velocities greater than $25^\circ/\text{sec}$, an initial acceleration of greater than $15^\circ/\text{sec}^2$, and a minimum duration of greater than 8 msec as saccades. Each movement record was reviewed manually, and saccades relevant to the task were identified. Artifact caused by blinking exhibits a distinct morphology and was removed from analysis by pattern recognition software. Sections of eye movement records during which subjects were not engaged in the task were identified by visual inspection and were excluded from all analyses.

Before participating in each eye movement experiment, subjects were given a verbal description of the task followed by a demonstration on the computer monitor while the procedure was described again. After the presentation, each subject was asked to explain the task in her own words. Subjects were allowed to proceed after they accurately described the nature of the task. Each task was preceded by the same 10-sec electronic calibration sequence.

All control subjects were tested once. Comparable data for the patient group were selected from the first test session, after a medication-free period of at least 10 days, either during baseline or while taking double-blind placebo ($n = 2$). To evaluate the temporal stability and practice effects of these tasks, we examined a subset of 15 girls who were tested during medication-free baseline and were then retested 3 to 9 weeks later while receiving double-blind placebo.

Smooth Pursuit Eye Movement

After calibration, the target moved horizontally back and forth over 30° for 5 cycles with a constant velocity of $17.0^\circ/\text{sec}$ and a 1.4-sec fixation period between ramps (a "trapezoidal" pattern). Prior to the task, subjects were instructed to keep their eyes on the target and follow it as closely as possible.

Saccades identified from movement records were classified as catch-up or anticipatory (Ross et al., 1998b). Saccades in the direction of target motion that decreased position error were classified as catch-up saccades. Saccades in the direction of target motion that increased position error were classified as anticipatory saccades. Closed-loop pursuit gain (ratio of eye velocity to target velocity) was also calculated from each movement record. Root mean square error reflects consistent global discrepancies between target and eye position and was calculated by squaring the difference between eye position and target position at each data point during all intervals of nonartificial pursuit tracking and then averaging the square root of these values.

Delayed Response Task

After electronic calibration, subjects were instructed to fixate on the central white square until it was turned off. During this fixation, a green square was illuminated for 50 msec at 1 of 4 positions, either 7.5° or 15° to the right or to the left of the central square in a pseudo-random sequence. The central white square was turned off 1,200 msec after the green target disappeared, signaling the initiation of an appropriate memory-guided saccade toward the location where the green target had appeared (Fig. 1). After 750 msec, the same green target was illuminated for 1,000 msec, allowing for a visually guided saccade toward the target if a memory-guided saccade had not been initiated. Saccades in the direction of the target that preceded the fixation square offset were scored as inhibition errors. Only saccades that exceeded 2° were scored; latencies of all saccade subtypes were calculated automatically. Accuracy of saccades was calculated as the ratio of the angular distance covered by the saccade to the angular distance from initial stimulus position to target position. For each of the 13 trials in this task, only the first saccadic response was scored in order to avoid confounding inhibition errors, which may represent premature "rehearsal" saccades, with memory-guided saccades.

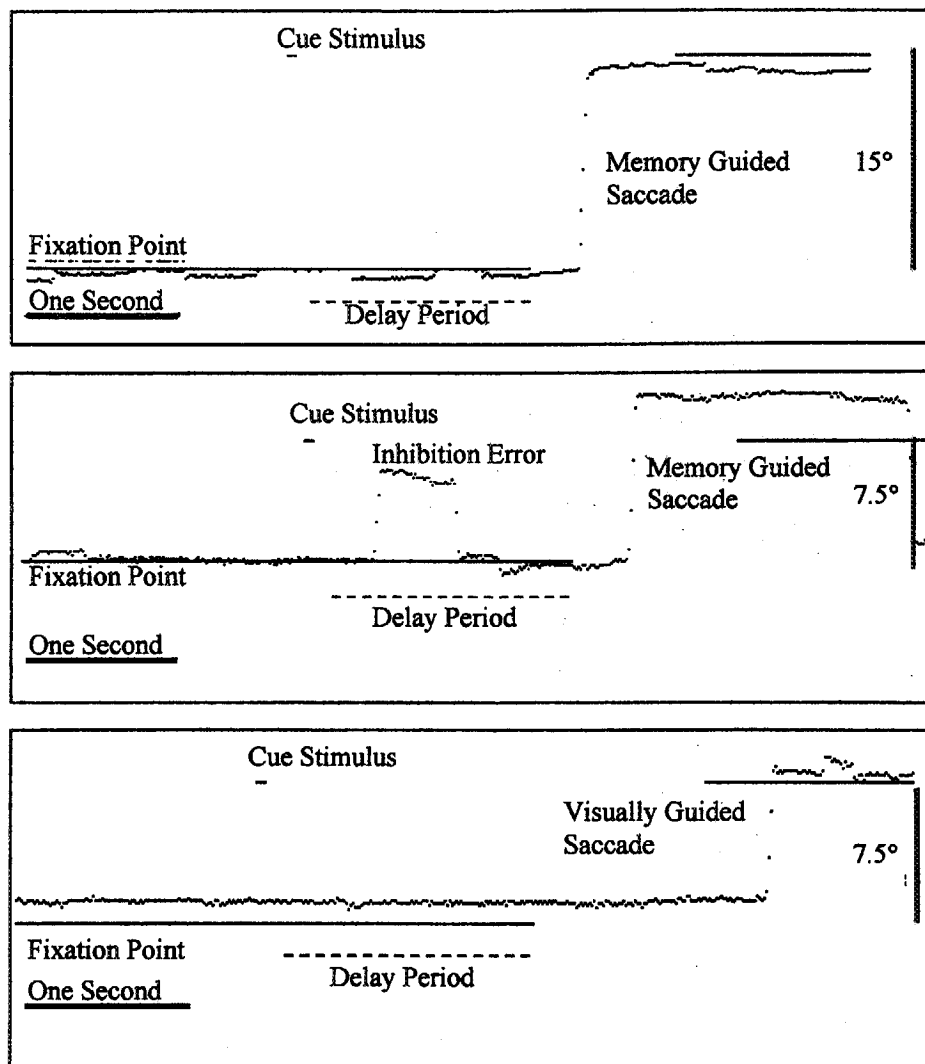


Fig. 1 Representative tracing from delayed response task. The top panel shows a correctly performed memory-guided saccade that follows the delay period; the middle panel shows an inhibition error (premature saccade) that was scored as an error, followed by a memory-guided saccade that was not scored; and the bottom panel shows an absence of response to the cue stimulus, followed by a visually guided saccade that was scored as an error.

Go-No Go Task

After the 10-sec electronic calibration, the fixation target returned to the center of the screen. After 2 sec, 4 other targets appeared. These targets were identical to the fixation target used for calibration (white squares, 0.3° on a side) and were located at 5° and 10° to the left and right of the center fixation target. The 4 targets and the center fixation point remained on the screen throughout the task.

The subject's task was to look at the targets cued by green rectangles and to ignore targets cued by red rectangles. Subjects were instructed to keep their eyes on the center fixation target until they saw a larger green rectangle appear over one of the white, smaller square targets. They were then instructed to look at that target and maintain fixation until they saw another green rectangle appear over a different target. The green rectangles represented the *go* cues, which remained visible for 300 msec each time. Subjects were instructed to ignore *no go* cues,

red rectangles that appeared over one of the targets for 300 msec. The *go* and *no go* cues were centered on the targets and extended 1.0° horizontally and 1.4° vertically, and they appeared in a pseudorandom sequence at intervals between 1.5 and 2.5 sec. Twelve *go* and 12 *no go* cues were presented during the task and all saccades, regardless of the cue, were scored.

Saccades with an amplitude of at least 3° were classified as 1 of 3 types: visually guided saccades to targets indicated by the *go* cue, saccades to targets indicated by the *no go* cue (commission errors), and saccades to a target not indicated by either the *go* or the *no go* cue (intrusion errors) (Fig. 2). The latencies of saccades to *go* or *no go* targets were measured automatically.

Ten records were analyzed by 3 trained raters who obtained excellent interrater reliability (mean intraclass correlation coefficient 0.94).

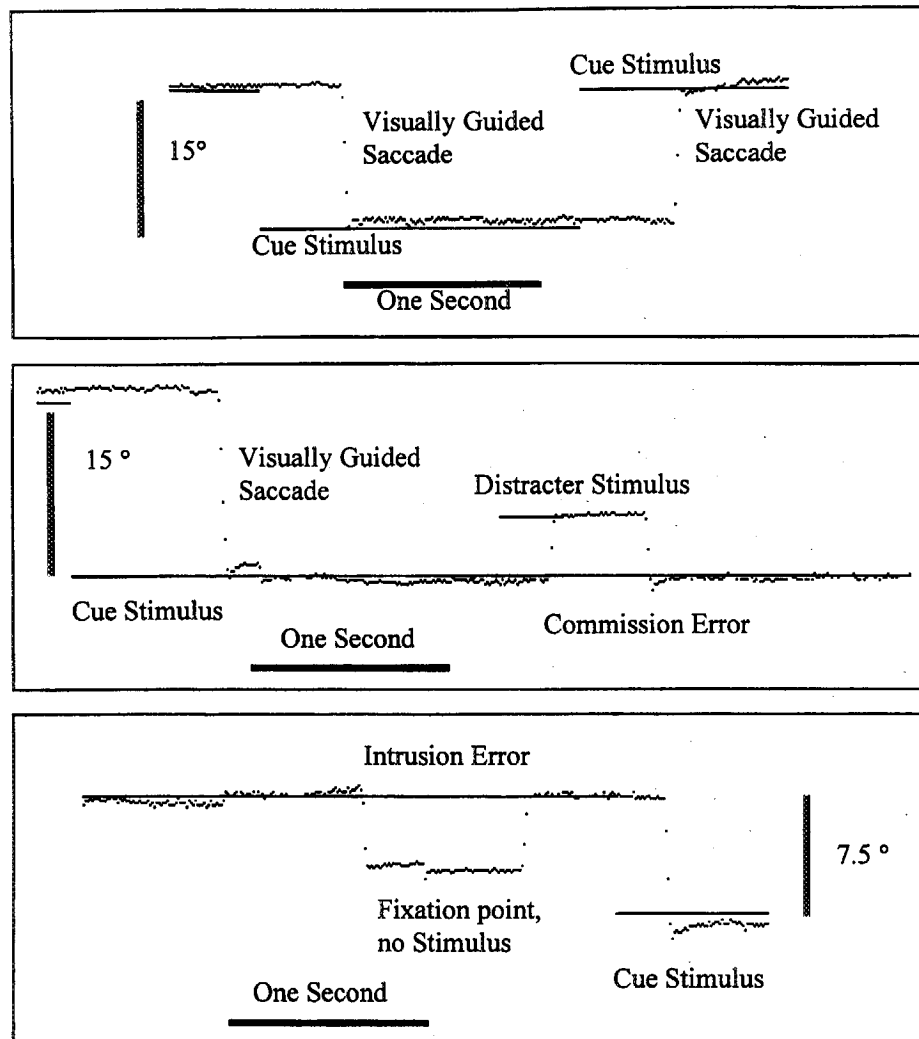


Fig. 2 Representative tracing from go-no go task. The top panel shows 2 correct visually guided saccades to go targets; the middle panel shows a commission error to the distracter stimulus (no go); and the bottom panel shows an intrusion error in the absence of go or no go stimuli.

Statistical Analysis

Because not all subjects completed all 3 tasks, repeated-measures analyses of variance could not be performed without excessive loss of data. Thus, dependent measures were compared between groups using unpaired *t* tests. Test-retest analyses used paired *t* tests. To decrease type I error, given the large number of comparisons, we defined statistical significance at $\alpha = .01$. All analyses were 2-tailed.

RESULTS

The order of testing was the same for all subjects, with smooth pursuit eye movement first, followed by go-no go and delayed response tasks. However, not all subjects completed all tasks, and data were unavailable for some tasks because of technical difficulties. Accordingly, results

for each task are reported separately (Tables 1–3). There were no significant group differences in age for any task.

As shown in Table 1, there were no significant differences among girls with ADHD and controls on any smooth pursuit measure.

Table 2 displays the results of the delayed response task. Girls with ADHD made significantly fewer memory-guided saccades than control subjects (31.6% versus 61.5%, $p < .001$). The percentage of working memory-guided trials on which there was a failure of inhibition was also significantly higher for girls with ADHD (55.2% versus 32.4%, $p = .01$). The number and latencies of visually guided saccades were also increased in girls with ADHD,

TABLE 1
Smooth Pursuit Eye Movements—17° per Second

Measure	ADHD (<i>n</i> = 32)		Control (<i>n</i> = 20)		<i>t</i>	<i>p</i>
	Mean	SD	Mean	SD		
Age (yr)	8.78	1.86	9.55	1.67	1.51	.14
Gain	0.70	0.15	0.74	0.17	0.81	.42
Root mean square error	5.20	2.76	3.95	2.11	1.72	.09
Total saccades/sec	3.50	1.13	4.15	2.87	1.14	.26
Anticipatory saccades/sec	1.70	0.76	1.87	0.97	0.73	.47
Catch-up saccades/sec	1.57	0.66	1.76	0.84	0.88	.38

although those differences were not statistically significant ($p = .06$ and $.02$, respectively).

As presented in Table 3, girls with ADHD made a significantly greater number of commission errors ($p < .0001$) and intrusion errors ($p < .004$) on go-no go testing compared with control subjects.

Repeated testing while on double-blind placebo ($n = 15$) demonstrated a decrease in commission errors from 5.1 ± 3.1 to 2.9 ± 3.3 ($p = .05$). Intrusion errors also decreased from 4.6 ± 5.4 to 2.5 ± 3.5 ($p = .09$). Number of visually guided saccades and latencies did not change substantially (11.2 ± 1.2 to 10.9 ± 1.5 [$p = .37$] and 433 ± 79 to 470 ± 135 [$p = .26$], respectively).

DISCUSSION

In this, the first examination of a battery of eye movement tasks in unmedicated girls with ADHD and age-matched control subjects, we found statistically robust abnormalities on the tasks that required inhibition and

working memory, i.e., go-no go and delayed response. In contrast, we did not detect significant differences in eye movement performance during smooth pursuit. The latter result is largely consistent with findings in a sample of 17 boys and 1 girl with ADHD who did not differ from controls on any smooth pursuit measure, except for root mean square error (Jacobsen et al., 1996). We also detected a nonsignificant tendency toward greater root mean square error in our patient sample. Our results differ from earlier findings of smooth pursuit deficits in hyperactive boys, although comparison is difficult because some studies predated the use of published diagnostic criteria (Bala et al., 1981; Shapira et al., 1980). A study of 17 boys and 3 girls with *DSM-III* ADHD found no differences in root mean square error but did find significant increases in "velocity arrests" during smooth pursuit at a higher target velocity ($28.6^\circ/\text{sec}$) than we used (Bylsma and Pivik, 1989). It is notable, however, that both our patient and control groups demonstrated deficient smooth pursuit relative to older subjects (Jacobsen et al., 1996), thus confirming the importance of maturation in eye movement tasks (Munoz et al., 1998; Ross et al., 1994b).

Despite the absence of significant differences in smooth pursuit, the girls with ADHD demonstrated robust deficiencies in both the delayed response and go-no go tasks. On delayed response, the girls with ADHD performed the required memory-guided saccades on 32% of trials, compared with 62% for the controls. However, the groups did not differ in response latency, confirming that once the working memory-guided decision was made, oculomotor processes were similar for the 2 groups. In the only other oculomotor study of the delayed response task in boys

TABLE 2
Delayed Response Task

Measure	ADHD (<i>n</i> = 28)		Control (<i>n</i> = 14)		<i>t</i>	<i>p</i>
	Mean	SD	Mean	SD		
Age (yr)	9.29	1.86	9.79	1.48	0.87	.39
Memory-guided saccades, no.	4.11	3.46	8.00	3.01	3.58	.0009
Latency (msec)	365.9	103.8	333.4	76.7	0.99	.33
Accuracy (%)	90.3	22.1	102.4	10.7	1.85	.07
Inhibition errors, no.	4.21	2.71	3.93	3.08	0.31	.76
Latency (msec)	527.7	200.3	592.6	213.8	0.97	.34
% of memory-guided saccades with inhibition errors (premature saccades)	55.2	27.7	32.4	23.2	2.64	.01
Visually guided saccades, no.	2.54	2.57	1.07	1.69	1.93	.06
Latency (msec)	360.9	140.9	210.8	83.7	2.39	.02
Accuracy (%)	114.3	68.4	104.6	13.2	0.34	.74

TABLE 3
Go-No Go Task

Measure	ADHD (<i>n</i> = 25)		Control (<i>n</i> = 20)		<i>t</i>	<i>p</i>
	Mean	SD	Mean	SD		
Age (yr)	9.18	1.73	9.95	1.57	1.55	.13
Visually guided saccades, no.	10.84	1.34	11.25	1.16	1.08	.29
Latency (msec)	433.5	98.3	465.3	79.5	1.17	.25
Commission errors, no.	5.32	3.22	1.95	1.70	4.19	.0001
Intrusion errors, no.	5.12	5.02	1.50	1.99	3.02	.004

with ADHD, the percentage of trials with inhibition failures was significantly elevated in patients ($p = .04$) (Ross et al., 1994a). Using the same formula to calculate percentage of trials with premature saccades, we confirmed their finding in girls with ADHD, although our rates of inhibition failures were substantially higher (55% and 32% in our patients and controls, respectively, versus 32% and 15% in theirs), in part because the subjects of the Ross et al. study were, on average, approximately 3 years older than ours.

There were also several statistical trends on the delayed response task that might reach significance with larger samples. Girls with ADHD were less accurate when performing memory-guided saccades ($p = .07$), and they made more late visually guided saccades (19.5% versus 8.2%, $p = .06$) at longer latencies than controls ($p = .02$).

In the go-no go task, patients did not differ significantly from controls in number of correct responses or in their latency, once again demonstrating similar oculomotor performance on the stimulus-driven aspects of the task. When required to inhibit a response, however, girls with ADHD committed more than twice as many commission errors ($p = .0001$). Even in the absence of any stimulus, the girls with ADHD produced more than 3 times as many intrusion errors ($p = .004$). Go-no go tasks have been extensively studied in ADHD (Pennington and Ozonoff, 1996; Shue and Douglas, 1992; Trommer et al., 1988, 1991; Vaidya et al., 1998), but an eye movement go-no go task has not been previously reported in ADHD. A neuroimaging study in normal adult males implicated the right prefrontal cortex in the no go process (Kawashima, 1996), and right prefrontal brain regions have also been implicated in imaging studies of boys with ADHD (Castellanos et al., 1996; Filipek et al., 1997).

Limitations

Our results must be considered in light of several limitations. Our sample sizes were not large, and some of our negative results may represent type II error. We are reporting results only for girls, rather than for combined groups of both sexes. Because of other studies that focused exclusively on girls, most of our subjects were female and we chose to leave out the few boys who were also studied. However, when 8 boys with ADHD were included along with 11 control boys, results on the go-no go task were identical. Not enough boys were analyzed on the delayed response task for meaningful comparisons.

Our eye movement tasks were brief in duration and number of trials. For example, each "complex" task consisted of 12 or 13 trials, and smooth pursuit lasted for less than 1 minute. Obtaining data from more trials might be expected to yield more statistically reliable results, thus also decreasing type II error.

We must also acknowledge a methodological limitation. Our software calculated saccadic accuracy as a percentage of the saccadic amplitude/distance traveled by the target. Unfortunately, undershoot and overshoot cancel each other out, which may have decreased our power to detect diagnostic differences in accuracy. Future studies should consider alternative approaches to quantify saccadic accuracy (Ross et al., 1998a).

Clinical Implications

As noted earlier, a pilot neuropsychological study of girls with ADHD found that the girls studied did not differ from controls in tasks that tap executive function, in contrast to boys with ADHD (Seidman et al., 1997). However, in that study, most of the patients (84%) were being treated with stimulant medications, which might have ameliorated executive function impairments. We conclude that unmedicated girls with ADHD exhibit impairments in executive function tasks, thereby supporting the notion that ADHD in girls is the same disorder as it is in boys (Biederman et al., 1999; Gaub and Carlson, 1997; Sharp et al., 1999), despite the differences in prevalence.

Finally, we must add one additional caveat. Because practice effects have not been found in smooth pursuit tasks in adults (Roy-Byrne et al., 1995) or in the oculomotor delayed response task in children (Ross et al., 1994a), we explored the possibility of using these measures in repeated-measures designs. Unfortunately, we found that go-no go commission errors decreased ($p = .05$) from the

first testing session to a subsequent session, thus indicating a substantial practice effect which may limit the utility of the oculomotor go-no go task for functional neuroimaging and other repeated-measures experiments.

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